

Patent claims:

1. A pharmaceutical salt of a pharmaceutical active compound and at least one sugar substitute with
5 the exception of the respective pharmaceutical salt of a sugar substitute and tramadol, (+)-tramadol, (-)-tramadol, (+)-demethyltramadol and (-)-demethyltramadol.
- 10 2. The pharmaceutical salt as claimed in claim 1, characterized in that the solubility of the salt in water is ≤ 250 mg/ml of water, preferably ≤ 200 mg/ml, particularly preferably ≤ 150 mg/ml, very particularly preferably ≤ 100 mg/ml.
- 15 3. The pharmaceutical salt as claimed in claim 1 or 2, characterized in that the salt-forming sugar substitute is saccharin, cyclamate or acesulfam, preferably saccharin.
- 20 4. The pharmaceutical salt as claimed in one of claims 1 to 3, characterized in that the salt-forming active compound is selected from the group consisting of the salt-forming analgesics,
25 antiobesity agents, analeptics, antihypoxemics, antirheumatics, opioid antagonists, anthelmintics, antiallergics, antiarrhythmics, antibiotics, antidementives (nootropics), antidiabetics, antiemetics, antivertiginous agents, antiepileptics,
30 antihypertensives, antihypotensives, antimycotics, antiinflammatories, antitussives, expectorants, arteriosclerosis agents, β -receptor blockers, calcium channel blockers, broncholytics, antiasthmatics, cholinergics, diuretics, circulation-promoting agents, weaning agents, geriatrics,
35 hypnotics, sedatives, immunomodulators, oral therapeutics, pharyngeal therapeutics, coronary agents, hypolipidemics, local anesthetics, neural

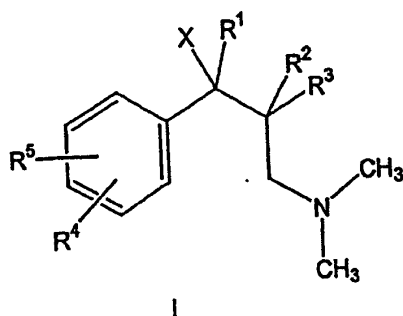
- therapeutics, gastric agents, intestinal agents,
migraine agents, muscle relaxants, anesthetics,
neuropathy preparations, ophthalmologicals,
otologicals, Parkinson agents,
5 psychopharmaceuticals, rhinologicals, sinusitis
agents, spasmolytics, platelet aggregation
inhibitors, tuberculosis agents, urologicals and
cytostatics.
- 10 5. The pharmaceutical salt as claimed in claim 4,
characterized in that the active compound is
selected from the group consisting of the salt-
forming analgesics, analeptics, antihypoxemics,
15 antiallergics, antiarrhythmics, antiemetics, anti-
vertiginous agents, antihypertensives, anti-
hypotensives, antitussives, expectorants, β -
receptor blockers, calcium channel blockers,
ophthalmologicals, otologicals, spasmolytics and
20 urologicals, preferably from the group consisting
of the salt-forming analgesics.
6. The pharmaceutical salt as claimed in claim 4 or
5, characterized in that the salt-forming
analgesic is selected from the group consisting of
25 the salt-forming opioids, the salt-forming opioid
analogs, ephedrine, chloroquine, lidocaine,
ethaverine, preglumetacin and triflupromazine.
7. The pharmaceutical salt as claimed in claim 6,
30 characterized in that the salt-forming opioid or
opioid analog is selected from the group
consisting of morphine, codeine, ethylmorphine,
diacetylmorphine, dihydrocodeine, etorphine,
hydrocodone, hydromorphone, levorphanol,
35 oxycodone, oxymorphone, pethidine, ketobemidone,
fentanyl, alfentanil, remifentanil, sufentanil,
levomethadone, levomethadyl, dextromoramide,
dextropropoxyphene, diphenoxylate, piritramide,
tilidine, buprenorphine, butorphanol, dezozine,

nalbuphine, nalorphine, pentazocine, nefopam, flupirtin and meptazinol.

5 8. The pharmaceutical salt as claimed in claim 7, characterized in that the salt-forming opioid is selected from the group consisting of morphine, codeine, hydrocodone, hydromorphone, oxycodone, tilidine, fentanyl and buprenorphine.

10 9. The pharmaceutical salt as claimed in one of claims 1 to 3, characterized in that the salt-forming active compound is a salt-forming compound of 1-phenyl-3-dimethylaminopropane compounds of the general formula I

15



in which

20 X is OH, F, Cl, H or an OCOR⁶ group,

R¹ is a C₁₋₄-alkyl group,

25 R² is H or a C₁₋₄-alkyl group and R³ is H or a straight-chain C₁₋₄-alkyl group or the radicals R² and R³ together form a C₄₋₇-cycloalkyl radical, and

30 if R⁵ is H, R⁴ is meta-O-Z where Z is H, C₁₋₃-alkyl, PO(O-C₁₋₄-alkyl)₂, CO(OC₁₋₅-alkyl), CONH-C₆H₄-(C₁₋₃-alkyl), CO-C₆H₄-R⁷, where R⁷ is ortho-OCOC₁₋₃-alkyl or meta- or para-CH₂N(R⁸)₂ where R⁸ is C₁₋₄-alkyl or 4-morpholino, or R⁴ is meta-S-C₁₋₃-alkyl, meta-Cl,

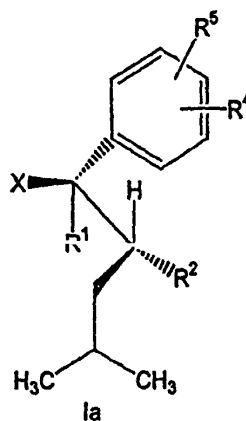
meta-F, meta-CR⁹R¹⁰R¹¹ where R⁹, R¹⁰, R¹¹ are H or F, ortho-OH, ortho-O-C₂₋₃-alkyl, para-F or para-CR⁹R¹⁰R¹¹ where R⁹, R¹⁰, R¹¹ are H or F, or if R⁵ is para-Cl, -F, -OH or -O-C₁₋₃-alkyl, R⁴ is meta-Cl, -F, -OH or -O-C₁₋₃-alkyl, or
5 R⁴ and R⁵ together are 3,4-OCH-CH- or 3,4-OCH=CHO-, R⁶ is C₁₋₃-alkyl,

10 in the form of their possible stereoisomers as racemates or diastereomerically pure enantiomers or in the form of mixtures of enantiomers, in which the respective enantiomers are present in nonequimolar amounts.

15 10. The pharmaceutical salt as claimed in claim 9, characterized in that X is OH, F, Cl or H, R¹ is a C₁₋₄-alkyl group, R² is H or CH₃ and R³ is H or CH₃ and if R⁵ is H, R⁴ is meta-O-C₁₋₃-alkyl, meta-OH, meta-S-C₁₋₃-alkyl, meta-F, meta-Cl, meta-CH₃, meta-
20 CF₂H, meta-CF₃ or para-CF₃ or if R⁵ is a para-Cl or -F, R⁴ is meta-Cl or -F, or R⁴ and R⁵ together are 3,4-OCH=CH-.

25 11. The pharmaceutical salt as claimed in claim 9 or 10, characterized in that the radicals R² and R³ have different meanings and the compounds of the general formula I as claimed in claim 9 are present in the form of their diastereomers having the configuration Ia

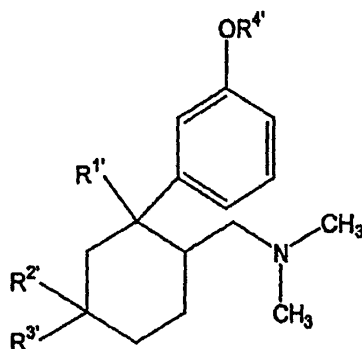
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12. The pharmaceutical salt as claimed in one of claims 9 to 11, characterized in that the salt-forming 1-phenyl-3-dimethylaminopropane compound is selected from the group consisting of
- 5
- (1RS,2RS)-3-(3-dimethylamino-1-hydroxy-1,2-dimethylpropyl)phenol,
- 10
- (-)-(1R,2R)-3-(3-dimethylamino-1-ethyl-2-methylpropyl)phenol,
- (+)-(1S,2S)-3-(3-dimethylamino-1-ethyl-2-methylpropyl)phenol,
- 15
- (2RS,3RS)-1-dimethylamino-3-(3-methoxyphenyl)-2-methylpentan-3-ol,
- 20
- (-)-(1S,2S)-3-(3-dimethylamino-1-ethyl-1-fluoro-2-methylpropyl)phenol,
- (+)-(1R,2R)-3-(3-dimethylamino-1-hydroxy-1,2-dimethylpropyl)phenol,
- 25
- (+)-(2R,3R)-1-dimethylamino-3-(3-methoxyphenyl)-2-methylpentan-3-ol and

(-)-(2S,3S)-1-dimethylamino-3-(3-methoxyphenyl)-
2-methylpentan-3-ol.

13. The pharmaceutical salt as claimed in one of
5 claims 1 to 3, characterized in that the salt-
forming active compound is a salt-forming compound
of 6-dimethylaminomethyl-1-phenylcyclohexane
compounds of the general formula II,



II

10

in which

R^{1'} is H, OH, Cl or F,

15

R^{2'} and R^{3'} are identical or different and are H,
C₁₋₄-alkyl, benzyl, CF₃, OH, OCH₂-C₆H₅, O-C₁₋₄-alkyl,
Cl or F with the proviso that at least one of the
radicals R^{2'} or R^{3'} is H,

20

R^{4'} is H, CH₃, PO(O-C₁₋₄-alkyl)₂, CO(O-C₁₋₅-alkyl),
CO-NH-C₆H₄-C₁₋₃-alkyl, CO-C₆H₄-R^{5'}, CO-C₁₋₅-alkyl, CO-
CHR^{6'}-NHR^{7'} or an unsubstituted or substituted
pyridyl, thienyl, thiazoyl [sic] or phenyl group,

25

R^{5'} is OC(O)C₁₋₃-alkyl in the ortho-position or CH₂-
N(R^{8'})₂ in the meta- or para-position, where R^{8'} is
C₁₋₄-alkyl or both radicals R^{8'} together with N are
the 4-morpholino radical, and

R^{6'} and R^{7'} are identical or different and are H or C₁₋₆-alkyl,

5 with the proviso that if both radicals R^{2'} and R^{3'} are H, R^{4'} is not CH₃ if R^{1'} is H, OH or Cl or R^{4'} is not H if R^{1'} is OH,

10 in the form of their possible stereoisomers as racemates or diastereomerically pure enantiomers or in the form of mixtures of enantiomers, in which the respective enantiomers are present in nonequimolar amounts.

15 14. The pharmaceutical salt as claimed in claim 13, characterized in that R^{1'} is H, OH or F.

20 15. The pharmaceutical salt as claimed in claim 13 or 14, characterized in that the compounds of the general formula II have a configuration in which the phenyl ring and the dimethylaminomethyl group are in each case arranged in an equatorial position to one another.

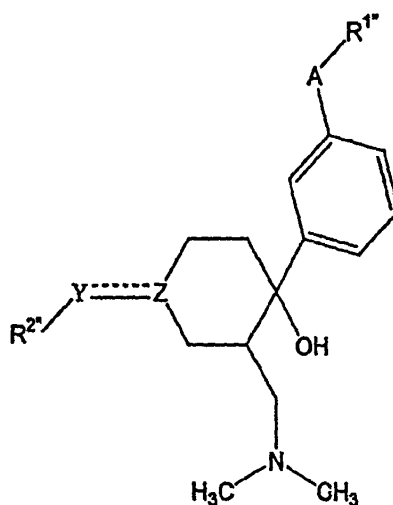
25 16. The pharmaceutical salt as claimed in one of claims 13 to 15, characterized in that the salt-forming 6-dimethylaminomethyl-1-phenylcyclohexane compound is selected from the group consisting of

30 (-)-(1R,2R)-3-(2-dimethylaminomethylcyclohexyl)-phenol,

 (1RS,3RS,6RS)-6-(dimethylaminomethyl)-1-(3-methoxyphenyl)cyclohexane-1,3-diol and

35 (1RS,3RS,6RS)-6-(dimethylaminomethyl)-1-(3-hydroxyphenyl)cyclohexane-1,3-diol.

17. The pharmaceutical salt as claimed in one of claims 1 to 3, characterized in that the salt-forming active compound is a salt-forming compound of 1-phenyl-2-dimethylaminomethylcyclohexan-1-ol compounds of the general formula III,



III

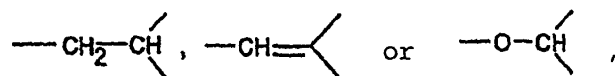
in which in each case

A is O or S,

R¹⁰ is H, C₁-6-alkyl, C₂-6-alkenyl, C₅-7-cycloalkyl or halogenated C₁-6-alkyl,

the group ---Y=Z<

is



R^{2''} is C₁₋₆-alkyl, C₂₋₆-alkenyl, C₅₋₇-cycloalkylmethyl, substituted or unsubstituted phenyl or substituted or unsubstituted benzyl,

5 in the form of their possible stereoisomers as racemates or diastereomerically pure enantiomers or in the form of mixtures of enantiomers, in which the respective enantiomers are present in nonequimolar amounts.

10

18. The pharmaceutical salt as claimed in claim 17, characterized in that R^{1''} is H, C₁₋₄-alkyl, 2'-methyl-2'-propenyl, cyclopentyl or fluoroethyl, with the proviso that R^{1''} is C₁₋₄-alkyl if A is S,

15

R^{2''} is C₁₋₄-alkyl, C₂₋₄-alkenyl, cyclopentylmethyl, phenyl, C₁₋₄-alkoxyphenyl, benzyl, C₁₋₄-alkylbenzyl, mono- or dihalogenated phenyl or mono- or dihalogenated benzyl.

20

19. The pharmaceutical salt as claimed in claim 17 or 18, characterized in that R^{1''} is H, methyl, ethyl, isopropyl, 2'-methyl-2'-propenyl, cyclopentyl or fluoroethyl, with the proviso that R^{1''} is methyl if A is S,

25

R^{2''} is methyl, propyl, 2'-methylpropyl, allyl, 2'-methyl-2'-propenyl, cyclopentylmethyl, phenyl, 3-methoxyphenyl, benzyl, 4-tert-butylbenzyl, 4-chlorobenzyl, 4-fluorobenzyl or 3,4-dichlorobenzyl.

30

20. The pharmaceutical salt as claimed in one of claims 17 to 19, characterized in that the compounds of the general formula III have a configuration in which the phenyl ring and the dimethylaminomethyl group are in each case arranged in an equatorial position to one another.

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21. The pharmaceutical salt as claimed in one of claims 17 to 20, characterized in that the salt-forming 1-phenyl-2-dimethylaminomethylcyclohexan-1-ol compound of the general formula III is selected from the group consisting of

(+)-(1R,2R,4S)-2-(dimethylaminomethyl)-4-(4-fluorobenzyloxy)-1-(3-methoxyphenyl)cyclohexanol,

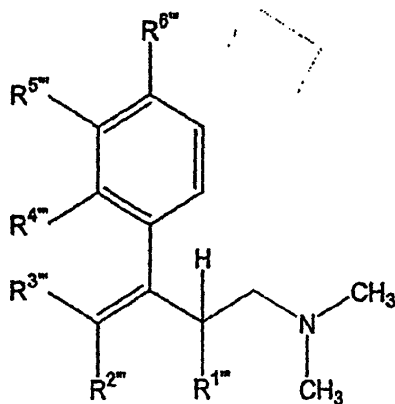
- 10 (+)-(1R,2R,4S)-2-dimethylaminomethyl-4-(4-chlorobenzyloxy)-1-(3-methoxyphenyl)cyclohexanol and

(+)-(1R,2R,4S)-3-[2-dimethylaminomethyl-4-(4-fluorobenzyloxy)-1-hydroxycyclohexyl]phenol.

15

22. The pharmaceutical salt as claimed in one of claims 1 to 3, characterized in that the salt-forming active compound is a salt-forming dimethyl-(3-arylbut-3-enyl)amine compound of the general formula IV, in which [sic]

20



IV

the radical R^{1'''} is C₁₋₅-alkyl and R^{2'''} is H or C₁₋₅-alkyl or R^{1'''} and R^{2'''} together are -(CH₂)₂₋₄-, -(CH₂)₂-CHR^{7'''} or -CH₂-CHR^{7'''}-CH₂-,

25

R^{3'''} is H or C₁₋₅-alkyl,

R^{4'''} is H, OH, C₁₋₄-alkyl, O-C₁₋₄-alkyl, O-benzyl, CF₃, O-CF₃, Cl, F or OR^{8'''},

5

R^{5'''} is H, OH, C₁₋₄-alkyl, O-C₁₋₄-alkyl, O-benzyl, CHF₂, CF₃, O-CF₃, Cl, F or OR^{8'''} and

10

R^{6'''} is H, OH, C₁₋₄-alkyl, O-C₁₋₄-alkyl, O-benzyl, CF₃, O-CF₃, Cl, F or OR^{8'''},

with the proviso that two of the radicals R^{4'''}, R^{5'''} or R^{6'''} are H, or

15

R^{4'''} and R^{5'''} together are -CH=C(R^{9'''})-O- or -CH=C(R^{9'''})-S-, with the proviso that R^{6'''} is H, or

R^{5'''} and R^{6'''} together are -CH=CH-C(OR^{10'''})=CH-, with the proviso that R^{4'''} is H,

20

R^{7'''} is C₁₋₈-alkyl, C₃₋₈-cycloalkyl, O-C₁₋₄-alkyl, O-benzyl, CF₃, Cl or F,

25

R^{8'''} is CO-C₁₋₅-alkyl, PO(O-C₁₋₄-alkyl)₂, CO-C₆H₄-R^{11'''}, CO(O-C₁₋₅-alkyl), CO-CHR^{12'''}-NHR^{13'''}, CO-NH-C₆H₃-(R^{14'''})₂ or an unsubstituted or substituted pyridyl, thienyl, thiazoyl [sic] or phenyl group,

30

R^{9'''} is H or C₁₋₄-alkyl,

R^{10'''} is H or C₁₋₃-alkyl,

35

R^{11'''} is OC(O)-C₁₋₃-alkyl in the ortho-position or CH₂-N-(R^{15'''})₂ in the meta- or para-position, where R^{15'''} is C₁₋₄-alkyl or both radicals R^{15'''} together with N form the 4-morpholino radical,

$R^{12''''}$ and $R^{13''''}$ are identical or different and are H, C_{1-6} -alkyl or C_{3-8} -cycloalkyl or $R^{12''''}$ and $R^{13''''}$ together are $-(CH_2)_{3-8}-$,

5 $R^{14''''}$ is H, OH, C_{1-7} -alkyl, O- C_{1-7} -alkyl, phenyl, O-aryl, CF_3 , Cl or F, with the proviso that the two radicals $R^{14''''}$ are identical or different,

10 in the form of their possible stereoisomers as racemates or diastereomerically pure enantiomers or in the form of mixtures of enantiomers, in which the respective enantiomers are present in nonequimolar amounts.

15 23. The pharmaceutical salt as claimed in claim 22, characterized in that $R^{1''''}$ is C_{1-3} -alkyl and $R^{2''''}$ is H or C_{1-3} -alkyl, or $R^{1''''}$ and $R^{2''''}$ together are $-(CH_2)_{2-4}-$ or $-(CH_2)_2-CHR^{7''''}$,

20 $R^{3''''}$ is H or C_{1-3} -alkyl,

$R^{4''''}$ is H, OH, CF_3 , Cl, F or $OR^{8''''}$,

25 $R^{5''''}$ is H, OH, C_{1-4} -alkyl, O- C_{1-4} -alkyl, O-benzyl, CHF_2 , CF_3 , Cl, F or $OR^{8''''}$ and

$R^{6''''}$ is H, OH, O- C_{1-4} -alkyl, O-benzyl, CF_3 , Cl, F or $OR^{8''''}$,

30 with the proviso that two of the radicals $R^{4''''}$, $R^{5''''}$ or $R^{6''''}$ are H, or

$R^{4''''}$ and $R^{5''''}$ together are $-CH=C(R^{9''''})-O-$ or $-CH=C(R^{9''''})-S-$, with the proviso that $R^{6''''}$ is H, or

35 $R^{5''''}$ and $R^{6''''}$ together are $-CH=CH-C(OR^{10''''})=CH-$, with the proviso that $R^{4''''}$ is H, and

$R^{7''''}$ is C_{1-4} -alkyl, CF_3 , Cl or F.

24. The pharmaceutical salt as claimed in claim 22 or 23, characterized in that $R^{1''''}$ is CH_3 or C_3H_7 and $R^{2''''}$ is H, CH_3 or CH_2CH_3 , or $R^{1''''}$ and $R^{2''''}$ together are $-(CH_2)_{2-3}-$ or $-(CH_2)_2-CHR^{7''''}$,

$R^{3''''}$ is H, CH_3 or CH_2CH_3 ,

$R^{4''''}$ is H or OH, $R^{5''''}$ is H, OH, OCH_3 , CHF_2 or $OR^{8''''}$ and $R^{6''''}$ is H, OH or CF_3 , with the proviso that two of the radicals $R^{4''''}$, $R^{5''''}$ or $R^{6''''}$ are H, or

$R^{4''''}$ and $R^{5''''}$ together are $-CH=C(CH_3)-S-$, with the proviso that $R^{6''''}$ is H, or

$R^{5''''}$ and $R^{6''''}$ together are $-CH=CH-C(OH)=CH-$, with the proviso that $R^{4''''}$ is H, and

$R^{8''''}$ is $CO-C_6H_4-R^{11''''}$ where $R^{11''''}$ is $OC(O)-C_{1-3}$ -alkyl in the ortho-position.

25. The pharmaceutical salt as claimed in one of claims 22 to 24, characterized in that

$R^{1''''}$ is CH_3 and $R^{2''''}$ is H or CH_3 or $R^{1''''}$ and $R^{2''''}$ together are $-(CH_2)_{2-3}-$ or $-(CH_2)_2-CH(CH_3)-$,

$R^{3''''}$ is H or CH_3 ,

$R^{4''''}$ is H, $R^{5''''}$ is OH or $OR^{8''''}$, $R^{6''''}$ is H, and $R^{8''''}$ is $CO-C_6H_4-R^{11''''}$ where $R^{11''''}$ is $OC(O)-CH_3$ in the ortho-position.

26. The pharmaceutical salt as claimed in one of claims 22 to 25, characterized in that the salt-forming dimethyl-(3-arylbut-3-enyl)amine compound present is trans-(-)-(1R)-3-[1-(2-dimethylamino-1-methylethyl)propenyl]phenol.

27. A medicament comprising at least one pharmaceutical salt as claimed in one of claims 1 to 26 and, if appropriate, physiologically tolerable excipients.
- 5 28. A medicament comprising at least one pharmaceutical salt as claimed in one of claims 6 to 26 for the control of pain.
- 10 29. A medicament comprising at least one pharmaceutical salt as claimed in one of claims 9 to 26 for the control of urinary incontinence.
- 15 30. The medicament as claimed in one of claims 27 to 29, characterized in that it are [sic] present formulated in the form of gels, chewing gums, juices, sprays, tablets, chewable tablets, coated tablets, powders, if appropriate filled into capsules, easily reconstitutable dry preparations, preferably in the form of gels, aqueous or oily
20 juices, sublingual sprays, tablets or chewable tablets.
- 25 31. The medicament as claimed in one of claims 27 to 29, characterized in that it is present formulated in multiparticulate form, preferably in the form of microtablets, microcapsules, granules, active compound crystals or pellets, particularly preferably in the form of microtablets, granules
30 or pellets, optionally filled into capsules or compressed to give tablets.
32. The medicament as claimed in one of claims 27 to 31, characterized in that the salt is present at
35 least partially in delayed-release form.
33. The medicament as claimed in claim 32, characterized in that delaying of the release is carried out by applying a release-delaying

coating, embedding in a release-delaying matrix, binding to an ion-exchange resin or by a combination of at least two of these methods.

- 5 34. The medicament as claimed in claim 33,
characterized in that the release-delaying coating
is based on a water-insoluble, optionally modified
natural or synthetic polymer, optionally in
10 combination with a customary plasticizer, or on a
natural, semisynthetic or synthetic wax or fat or
fatty alcohol or a mixture of at least two of
these components.
- 15 35. The medicament as claimed in claim 33,
characterized in that the matrix is based on a
hydrophilic matrix material, preferably
hydrophilic polymers, particularly preferably on
cellulose ethers, cellulose esters and/or acrylic
resins, very particularly preferably on
20 ethylcellulose, hydroxypropylmethylcellulose,
hydroxypropylcellulose, hydroxymethylcellulose,
poly(meth)acrylic acid and/or their salts,
amides and/or esters.
- 25 36. The medicament as claimed in claim 33,
characterized in that the matrix is based on a
hydrophobic matrix material, preferably
hydrophobic polymers, waxes, fats, long-chain
fatty acids, fatty alcohols or appropriate esters
30 or ethers or their mixtures, particularly
preferably on mono- or diglycerides of C₁₂-C₃₀
fatty acids and/or C₁₂-C₃₀-fatty alcohols and/or
waxes or their mixtures.
- 35 37. The medicament as claimed in one of claims 27 to
36, characterized in that it has a protective
coating, preferably an enteric protective coating.

38. The use of at least one pharmaceutical salt as claimed in one of claims 6 to 26 for the production of a medicament for the control of pain.

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39. The use of at least one pharmaceutical salt as claimed in one of claims 9 to 26 for the production of a medicament for the treatment of urinary incontinence.